September 30, 1952

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Dear Max:

Thank you for the interesting reports on the Royaumont meetings and on Dr. Vogt's work. We shall be looking forward to seeing and discussing Appleyard's program, but a few questions can be brought up meanwhile.

Concerning the suggestion of two stages in zygote formation, I have always wondered from Tom's work, whether the first is not merely a non-specific agglutination, which requires some nutrient supply to proceed to significant combinations (viz. stable to dilution and dispersion). Tom seems to be agreeable to this interpretation. As you know, Nelson is working with me for the year, and has started kinetic studies on the Hfr system. It is already apparent that cell mixtures do nothing very interesting in salts medium, but whether actual growth is needed is undecided. In this system, clumping seems to play a relatively unimportant role as compared to its probable effect on the earlier material. We have not been working on this long enought to give a clear picture, and I cannot yet predict whether a distinctive problem will shape up along the lines of Kaiser's suggested thesis. We will be unable to avoid studying the physiological essentials for Hfr combination, but this will not be based on the two-stage concept as such. If Kaiser does formulate a different approach with his material, we will, of course, do our best to leave a clear field for him. I especially welcome your suggestion for closer contact and exchange of information, which should obviate any difficulties in this respect.

Your letter said something about marked lambda. We have not been entirely satisfied with the recombination evidence for the chromosomal-prolambda theory: not because of ambiguities in recombination analysis per se, however. We find heterozygous diploids from which lysogenicity/non-lysogenicity segregates. One may infer that the material basis for this is the chromosomal prolambda, but the determinant might be as different from lambda as K is from kappa. We are inclined to prefer the c. -p. theory, as it seems to provide a better basis for phage-mediated genetic transductions, but cannot regard the evidence as conclusive. If we could introduce a mutant lambda' so as to obtain diploids which segregate lambda/lambda' in the same linked fashion as lambda/nolambda, the chromosomal localization of part of the virus would be strengthened. Unfortunately, the most characteristic mutant of lambda, lambda-2, does not induce lysogenicity in our stocks, and we have not yet discovered a suitable mutant.

In this connection, we have been looking over a number of potential host strains, many of them accumulated as interfertile with K-12. It looks as if smooth-rough variation has not been sufficiently emphasized as a [redacted] of phage-susceptibility.

There is some circumstantial evidence that lambda and T1, T2, etc. are "rough" -specific phages, judging from the occurrence of susceptible, rough variants in aged cultures of some of our apparently smooth resistant strains. We are therefore looking for smooth-specific phages to permit a more systematic isolation of the rough variants. I hope our correspondence can suggest suitable criteria for a division of labor. It is fairly obvious that we are less well equipped to do adsorption, growth, etc. studies on phage than genetic studies on their bacterial hosts, and it is possible that the converse holds at Caltech.

Sincerely,

Joshua Lederberg

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